Applicants have amended their claims in order to more particularly point out and distinctly claim their invention. Thus, the limits of originally filed claim 9 have been incorporated into claims 28 and 29. Since claims 5 and 9 fail to further limit amended claim 28, they have been presently cancelled. No new matter has been added.

Formulation claims 16-17, 20-21 and 29 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 5,171,566 (Mizushima), the examiner correctly asserting that the claims appear to be product-by-process claims. For the same reason claim 29 is rejected under 35 U.S.C. § 102 as being anticipated by U.S. Patent 5,338,761 (Nakajima et al.). Reconsideration of both grounds of rejection is requested in light of the amendment *supra* and the following remarks.

Applicants note that independent composition claim 29 has now been substantially restricted to a selection which consists essentially of the components (a) to (d). If one of these components is absent, the composition, which is a nanodispersion, cannot be formed in the absence of high shear or cavitation forces. Applicants emphasize that **ethanol** (component (d)) is an **essential element** of their claim, which is not disclosed either in U.S. Patent 5,171,566 (Mizushima et al.) or in U.S. Patent 5,338,761 (Nakajima et al.), or in any of the other cited documents. In contradistinction, Mizushima and Nakajima use **glycerol**, which is known by one skilled in the art to be suitable to act as a homogenizing agent when using high shear forces, the methods which are applied in both references. Consequently, the composition according to claim 29 is clearly distinct from the compositions obtained by Mizushima or Nakajima. The same applies to claims 16-17 and to claims 20-21, which depend on claim 29 and further limit it.

Reconsideration and withdrawal of the rejection of claims 16-17, 20-21 and 29 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 5,171,566 (Mizushima et al.), and of claim 29 under 35 U.S.C. § 102 as being anticipated by U.S. Patent 5,338,761 (Nakajima et al.) is respectfully solicited in light of the remarks *supra*.

Claims 2, 5-6, 9-10, 15-21, 24 and 28-29 are rejected under 35 U.S.C. § 102(b) as being anticipated, or in the alternative as obvious over U.S. Patent 5,633,226 (Owen et al.). Reconsideration of both grounds of rejection is requested in light of the amendment *supra* and the following remarks.

Initially applicants note that both independent method claim 28 and independent composition claim 29 have now been substantially restricted the same way to a selection which consists essentially of the components (a) to (d). Applicants again emphasize that **ethanol** (component (d)) is an **essential lement** of their claim. Ethanol is not disclosed in U.S. Patent 5,633,226 (Owen et al.). Rather, Owen et al. discloses water-in-oil (rather than oil-in-water) microemulsions comprising

(a) an aqueous phase,

(b) a pharmaceutically acceptable oil or mixtures thereof,

(c) an oil-dispersible surfactant and

(d) a water-soluble biologically active material or combination of materials (col. 4, lines 49-54). In particular Owen uses a water / saline buffer solution **without ethanol** (claimed component (d)) as an aqueous phase. Further, with regard to the process, Owen teaches to preferably dissolve the active material in the aqueous phase and then add this aqueous phase to a mixture of the oil and the surfactant (col.10, line 66 to col. 11, line 3). A vortex mixer is used in all the examples. In contrast thereto independent method claim 28 requires as step (α) mixing the components (a)-(d) in conventional stirring apparatus until a homogeneous clear liquid is obtained, wherein component (c) comprises a lipophilic component which is a natural or synthetic or a partially synthetic C_4-C_{18}tri-glyceride, and a lipophilic pharmaceutical active agent, in which any pharmaceutically active agent is lipophilic and is always present as component (c), and (β) adding the liquid obtained in step (α) to the water phase, wherein (β) is carried out in the absence of high shear or cavitation forces. Thus there are clear compositional and process differences from Owen which preclude a rejection under 35 U.S.C. § 102.

With respect to the instant claim rejection under 35 U.S.C. 103(a) as obvious over Owen et al., it would appear advisable to consider something of the nature of the subject matter of the present invention in comparison to Owen:

The present invention in amended claim 29 provides an aqueous nanodispersion of a lipophilic pharmaceutical active agent, which consists essentially of 4 components (a) - (d). Without any of the 4 components, the disclosed nanodispersion cannot be obtained. The lipophilic component (c) consists of a **lipophilic** C_4-C_{18}triglyceride and a **lipophilic** pharmaceutical active agent. And component (d) consists necessarily of **ethanol**.

In contrast thereto Owen teaches a microemulsion composition with a **water soluble** biological active material; see claims 10 a) or 1 a) "...an **ffectiv amount** of a biologically **active component that is**

water soluble;". Applicants respectfully note that claim 10 does not recite "a suitable pharmaceutical active material" as asserted by the examiner. Owen's disclosure is clearly addressed to water soluble active materials such as water soluble proteins or peptides.

Owen further discloses an aqueous phase as another component. No suggestion is given in the entire disclosure to ever use a monohydrolic alcohol. Applicants note that polyhydrolic alcohols like glycerin and propylene glycol are not excluded, but would like to stress that Owen et al. clearly demotivates one from using any monohydrolic alcohol in their microemulsions. Note col.5, lines 44-47, and col.7, lines 53-55. Moreover, in all the working examples, only a water/saline buffer solution in the absence of any polyhydrolic alcohol has been used as the aqueous phase. In contradistinction thereto, in amended claims 28 and 29, component (d) now is defined to be ethanol.

While the examiner has further objected to the "open ended claims" type, applicants' would like to point out that amended composition claim 29 now reads as "An aqueous nanodispersion of a lipophilic pharmaceutical active agent, which consists essentially of...". Independent method claim 28 was amended in an analogous way.

Reconsideration and withdrawal of the rejection of claims 2, 6, 10, 15-21, 24 and 28-29 under 35 U.S.C. § 102(b) as being anticipated, or in the alternative as obvious over U.S. Patent 5,633,226 (Owen et al.) is respectfully solicited in light of the remarks *supra*.

Claims 2, 5-6, 9-10, 15-21, 24 and 28-29 are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 95/16441. WO 95/16441 discloses ultramicroemulsions with esters of Apocarotinols **in water**. As coemulsifying solvents are disclosed only alcohol-**esters** with at least 3 carbon atoms (see pg. 20, paragraph 5 ff.), but preferred are long-chain alcohol-esters. No free alcohol is disclosed, much less a mono-alcohol such as ethanol.

Regarding the examiner's comment on page 6, "...an aqueous phase such as ethanol (see example 14-16, and claims 1-3)...", applicants would like to clarify that the word "ethanol" appears only once in the disclosure, namely on page 31, where is stated "...Aceton / Ethanol 1:1...". It further states that this mixture solely is used to **seal** ("...1:1 **verschlossen** werden...") the pharmaceutical capsules after they are filled with the micropellets or granules. As a consequence, any ethanol or acetone will be quickly evaporated. This portion of the disclosure has nothing to do with microemulsions. Likewise, claims 1-3, pointed to by the examiner are totally silent about ethanol or any alcohol for that matter.

Reconsideration and withdrawal of the rejection of claims 2, 6, 10, 15-21, 24 and 28-29 under 35 U.S.C. § 102(b) as being anticipated by WO 95/16441 is respectfully solicited in light of the remarks *supra*.

Since there are no other grounds of objection or rejection, passage of this application to issue with claims 2, 6, 10, 15-21, 24 and 28-29 is earnestly solicited.

Applicants submit that the present application is in condition for allowance. In the event that minor amendments will further prosecution, Applicants request that the examiner contact the undersigned representative.

Respectfully submitted,

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